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 NEWS  2  Sep 17   IMSworld Pharmaceutical Company Directory name change
                   to PHARMASEARCH
 NEWS  3  Oct 09   Korean abstracts now included in Derwent World Patents
                   Index
 NEWS  4  Oct 09   Number of Derwent World Patents Index updates increased
 NEWS  5  Oct 15   Calculated properties now in the REGISTRY/ZREGISTRY File
 NEWS  6  Oct 22   Over 1 million reactions added to CASREACT
 NEWS  7  Oct 22   DGENE GETSIM has been improved
 NEWS  8  Oct 29   AAASD no longer available
 NEWS  9  Nov 19   New Search Capabilities  USPATFULL and USPAT2
 NEWS 10  Nov 19   TOXCENTER(SM) - new toxicology file now available on STN
 NEWS 11  Nov 29   COPPERLIT now available on STN
 NEWS 12  Nov 29   DWPI revisions to NTIS and US Provisional Numbers
 NEWS 13  Nov 30   Files VETU and VETB to have open access
 NEWS 14  Dec 10   WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
 NEWS 15  Dec 10   DGENE BLAST Homology Search
 NEWS 16  Dec 17   WELDASEARCH now available on STN
 NEWS 17  Dec 17   STANDARDS now available on STN
 NEWS 18  Dec 17   New fields for DPCI
 NEWS 19  Dec 19   CAS Roles modified
 NEWS 20  Dec 19   1907-1946 data and page images added to CA and CAplus
 NEWS 21  Jan 25   BLAST(R) searching in REGISTRY available in STN on the Web
 NEWS 22  Jan 25   Searching with the P indicator for Preparations
 NEWS 23  Jan 29   FSTA has been reloaded and moves to weekly updates
 NEWS 24  Feb 01   DKILIT now produced by FIZ Karlsruhe and has a new update
                   frequency
 NEWS 25  Feb 19   Access via Tymnet and SprintNet Eliminated Effective 3/31/02
 NEWS 26  Mar 08   Gene Names now available in BIOSIS

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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=> s formoterol
L1        2604 FORMOTEROL

=> s fluticasone propionate
L2        3662 FLUTICASONE PROPIONATE

=> s l1 ad l2
MISSING OPERATOR L1 AD
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l1 and l2
L3         179 L1 AND L2

=> s sodium chloride or saline
L4      600269 SODIUM CHLORIDE OR SALINE

=> s citric acid
L5      140111 CITRIC ACID

=> s l3 and l4 and l5
L6           3 L3 AND L4 AND L5

=> d l6 1-3

L6   ANSWER 1 OF 3  USPATFULL
AN     2001:187017  USPATFULL
TI     Closure-cap and container as a two-chamber cartridge for nebulisers for
       producing aerosols and active substance formulations, suitable for
       storage
IN     Hochrainer, Dieter, Bingen, Germany, Federal Republic of
       Zierenberg, Bernd, Bingen, Germany, Federal Republic of
PI     US 2001032643      A1   20011025
AI     US 2001-871500     A1   20010531 (9)
```

RLI Continuation of Ser. No. US 1999-416476, filed on 12 Oct 1999, PENDING
PRAI DE 1998-19847968 19981017
DE 1998-19847970 19981017
DT Utility
FS APPLICATION
LN.CNT 1291
INCL INCLM: 128/200.210
INCLS: 604/415.000
NCL NCLM: 128/200.210
NCLS: 604/415.000
IC [7]
ICM: A61M005-32
ICS: A61B019-00

L6 ANSWER 2 OF 3 USPATFULL
AN 2001:90260 USPATFULL
TI Fatty acid-pharmaceutical agent conjugates
IN Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
Swindell, Charles S., Merion, PA, United States
Shashoua, Victor E., Brookline, MA, United States
PI US 2001002404 A1 20010531
AI US 2000-730450 A1 20001205 (9)
RLI Continuation of Ser. No. US 1996-651428, filed on 22 May 1996, ABANDONED
DT Utility
FS APPLICATION
LN.CNT 2511
INCL INCLM: 514/560.000
INCLS: 514/558.000
NCL NCLM: 514/560.000
NCLS: 514/558.000
IC [7]
ICM: A61K031-20
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 3 OF 3 USPATFULL
AN 1998:98932 USPATFULL
TI DHA-pharmaceutical agent conjugates of taxanes
IN Shashoua, Victor E., Brookline, MA, United States
Swindell, Charles S., Merion, PA, United States
Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
PA Neuromedica, Inc., Conshohocken, PA, United States (U.S. corporation)
PI US 5795909 19980818
AI US 1996-651312 19960522 (8)
DT Utility
FS Granted
LN.CNT 2451
INCL INCLM: 514/449.000
INCLS: 514/549.000
NCL NCLM: 514/449.000
NCLS: 514/549.000
IC [6]
ICM: A61K031-335
ICS: A61K031-22
EXF 514/449; 514/549
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
=> s l4 and l3
L7          10 L4 AND L3

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8          10 DUP REM L7 (0 DUPLICATES REMOVED)

=> d l8 1-19

L8   ANSWER 1 OF 10  USPATFULL
AN     2002:30480  USPATFULL
TI     Phospholipid-based powders for inhalation
IN     Weers, Jeffry G., Half Moon Bay, CA, UNITED STATES
       Tarara, Thomas E., Burlingame, CA, UNITED STATES
       Clark, Andrew, Half Moon Bay, CA, UNITED STATES
PI     US 2002017295      A1   20020214
AI     US 2001-888311     A1   20010622 (9)
PRAI   US 2000-216621      20000707 (60)
DT     Utility
FS     APPLICATION
LN.CNT 1103
INCL   INCLM: 128/203.120
       INCLS: 424/043.000
NCL    NCLM:  128/203.120
       NCLS:  424/043.000
IC     [7]
       ICM: A61K009-00
       ICS: A61K009-14
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8   ANSWER 2 OF 10  USPATFULL
AN     2001:217988  USPATFULL
TI     Stabilized preparations for use in metered dose inhalers
IN     Weers, Jeffry G., San Diego, CA, United States
       Schutt, Ernest G., San Diego, CA, United States
       Dellamary, Luis A., San Marcos, CA, United States
       Tarara, Thomas E., San Diego, CA, United States
       Kabalnov, Alexey, Corvallis, OR, United States
PI     US 2001046474      A1   20011129
AI     US 2001-862764     A1   20010521 (9)
RLI    Division of Ser. No. US 1998-218212, filed on 22 Dec 1998, PENDING
       Continuation of Ser. No. WO 1998-US20615, filed on 29 Sep 1998, UNKNOWN
       Continuation-in-part of Ser. No. US 1998-133848, filed on 14 Aug 1998,
       ABANDONED Continuation-in-part of Ser. No. US 1998-106932, filed on 29
       Jun 1998, ABANDONED
PRAI   US 1997-60337       19970929 (60)
DT     Utility
FS     APPLICATION
LN.CNT 2850
INCL   INCLM: 424/045.000
NCL    NCLM:  424/045.000
IC     [7]
       ICM: A61L009-04
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8   ANSWER 3 OF 10  USPATFULL
AN     2001:212586  USPATFULL
TI     In vivo delivery methods and compositions
IN     Kensey, Kenneth R., Malvern, PA, United States
PI     US 2001044584      A1   20011122
```

AI US 2001-819924 A1 20010328 (9)
RLI Continuation-in-part of Ser. No. US 2000-727950, filed on 1 Dec 2000, PENDING Continuation-in-part of Ser. No. US 2000-628401, filed on 1 Aug 2000, PENDING Continuation-in-part of Ser. No. US 2000-501856, filed on 10 Feb 2000, PENDING Continuation-in-part of Ser. No. US 1999-439795, filed on 12 Nov 1999, PENDING Continuation-in-part of Ser. No. US 1997-919906, filed on 28 Aug 1997, GRANTED, Pat. No. US 6019735
DT Utility
FS APPLICATION
LN.CNT 2120
INCL INCLM: 600/504.000
INCLS: 600/573.000; 604/066.000; 604/067.000
NCL NCLM: 600/504.000
NCLS: 600/573.000; 604/066.000; 604/067.000
IC [7]
ICM: A61B005-00

L8 ANSWER 4 OF 10 USPATFULL
AN 2001:187017 USPATFULL
TI Closure-cap and container as a two-chamber cartridge for nebulisers for producing aerosols and active substance formulations, suitable for storage
IN Hochrainer, Dieter, Bingen, Germany, Federal Republic of
Zierenberg, Bernd, Bingen, Germany, Federal Republic of
PI US 2001032643 A1 20011025
AI US 2001-871500 A1 20010531 (9)
RLI Continuation of Ser. No. US 1999-416476, filed on 12 Oct 1999, PENDING
PRAI DE 1998-19847968 19981017
DE 1998-19847970 19981017
DT Utility
FS APPLICATION
LN.CNT 1291
INCL INCLM: 128/200.210
INCLS: 604/415.000
NCL NCLM: 128/200.210
NCLS: 604/415.000
IC [7]
ICM: A61M005-32
ICS: A61B019-00

L8 ANSWER 5 OF 10 USPATFULL
AN 2001:149472 USPATFULL
TI PROCESS AND DEVICE FOR INHALATION OF PARTICULATE MEDICAMENTS
IN VAN OORT, MICHIEL MARY, DURHAM, NC, United States
SACCHETTI, MARK JOSEPH, RALEIGH, NC, United States
PI US 2001018916 A1 20010906
AI US 1998-155388 A1 19980928 (9)
WO 1997-EP1560 19970325
None PCT 102(e) date
PRAI GB 1996-6677 19960329
DT Utility
FS APPLICATION
LN.CNT 775
INCL INCLM: 128/203.120
NCL NCLM: 128/203.120
IC [7]
ICM: A61M015-00
ICS: A61M016-10

L8 ANSWER 6 OF 10 USPATFULL

AN 2001:90260 USPATFULL
TI Fatty acid-pharmaceutical agent conjugates
IN Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
Swindell, Charles S., Merion, PA, United States
Shashoua, Victor E., Brookline, MA, United States
PI US 2001002404 A1 20010531
AI US 2000-730450 A1 20001205 (9)
RLI Continuation of Ser. No. US 1996-651428, filed on 22 May 1996, ABANDONED
DT Utility
FS APPLICATION
LN.CNT 2511
INCL INCLM: 514/560.000
INCLS: 514/558.000
NCL NCLM: 514/560.000
NCLS: 514/558.000
IC [7]
ICM: A61K031-20
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 7 OF 10 USPATFULL
AN 2001:190709 USPATFULL
TI Stabilized preparations for use in metered dose inhalers
IN Weers, Jeffry G., San Diego, CA, United States
Schutt, Ernest G., San Diego, CA, United States
Dellamary, Luis A., San Marcos, CA, United States
Tarara, Thomas E., San Diego, CA, United States
Kabalnov, Alexey, Corvallis, OR, United States
PA Inhale Therapeutic Systems, Inc., San Carlos, CA, United States (U.S. corporation)
PI US 6309623 B1 20011030
AI US 1998-218212 19981222 (9)
RLI Continuation of Ser. No. WO 1998-US20615, filed on 29 Sep 1998
Continuation-in-part of Ser. No. US 1998-133848, filed on 14 Aug 1998, now abandoned Continuation-in-part of Ser. No. US 1998-106932, filed on 29 Jun 1998, now abandoned
PRAI US 1997-60337 19970929 (60)
DT Utility
FS GRANTED
LN.CNT 2644
INCL INCLM: 424/045.000
INCLS: 424/046.000; 424/489.000
NCL NCLM: 424/045.000
NCLS: 424/046.000; 424/489.000
IC [7]
ICM: A61K009-12
EXF 424/45; 424/46; 424/489
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 8 OF 10 USPATFULL
AN 2001:86043 USPATFULL
TI Medicament carrier with agglomerated large medicament particles and related method of manufacture thereof
IN Van Oort, Michiel Mary, Durham, NC, United States
Sacchetti, Mark Joseph, Raleigh, NC, United States
PA Glaxo Wellcome Inc., Research Triangle Park, NC, United States (U.S. corporation)
PI US 6245339 B1 20010612
WO 9804308 19980205

AI US 1999-230613 19990128 (9)
WO 1997-EP4128 19970730
19990128 PCT 371 date
19990128 PCT 102(e) date
PRAI GB 1996-16047 19960731
DT Utility
FS GRANTED
LN.CNT 938
INCL INCLM: 424/400.000
INCLS: 128/203.120; 128/203.130; 128/203.150; 128/203.190; 128/203.210; 128/203.230
NCL NCLM: 424/400.000
NCLS: 128/203.120; 128/203.130; 128/203.150; 128/203.190; 128/203.210; 128/203.230
IC [7]
ICM: A61K009-00
ICS: A61M015-00; A61M016-10; A61M016-00
EXF 424/400; 128/203.12; 128/203.13; 128/203.15; 128/203.19; 128/203.21; 128/203.23

L8 ANSWER 9 OF 10 USPATFULL
AN 2000:76042 USPATFULL
TI Metering apparatus
IN Dwivedi, Sarvajna Kumar, San Diego, CA, United States
Roberts, II, William Leroy, Apex, NC, United States
Sacchetti, Mark Joseph, Raleigh, NC, United States
Van Oort, Michiel Mary, Durham, NC, United States
PA Glaxo Wellcome Inc., Research Triangle Park, NC, United States (U.S. corporation)
PI US 6076522 20000620
WO 9744080 19971127
AI US 1998-180648 19981112 (9)
WO 1997-EP2594 19970522
19981112 PCT 371 date
19981112 PCT 102(e) date
PRAI GB 1996-10821 19960523
DT Utility
FS Granted
LN.CNT 1090
INCL INCLM: 128/203.150
INCLS: 128/203.120
NCL NCLM: 128/203.150
NCLS: 128/203.120
IC [7]
ICM: A61M015-00
EXF 128/203.15; 128/203.12; 128/203.21

L8 ANSWER 10 OF 10 USPATFULL
AN 1998:98932 USPATFULL
TI DHA-pharmaceutical agent conjugates of taxanes
IN Shashoua, Victor E., Brookline, MA, United States
Swindell, Charles S., Merion, PA, United States
Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
PA Neuromedica, Inc., Conshohocken, PA, United States (U.S. corporation)
PI US 5795909 19980818
AI US 1996-651312 19960522 (8)
DT Utility
FS Granted
LN.CNT 2451

INCL INCLM: 514/449.000
INCLS: 514/549.000
NCL NCLM: 514/449.000
NCLS: 514/549.000
IC [6]
ICM: A61K031-335
ICS: A61K031-22
EXF 514/449; 514/549
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 2 ab bib kwic

L8 ANSWER 2 OF 10 USPATFULL
AB Stabilized dispersions are provided for the delivery of a bioactive agent to the respiratory tract of a patient. The dispersions preferably comprise a plurality of perforated microstructures dispersed in a suspension medium that typically comprises a hydrofluoroalkane propellant. As density variations between the suspended particles and suspension medium are minimized and attractive forces between microstructures are attenuated, the disclosed dispersions are particularly resistant to degradation, such as, by settling or flocculation. In particularly preferred embodiments, the stabilized dispersions may be administered to the lung of a patient using a metered dose inhaler.
AN 2001:217988 USPATFULL
TI Stabilized preparations for use in metered dose inhalers
IN Weers, Jeffry G., San Diego, CA, United States
Schutt, Ernest G., San Diego, CA, United States
Dellamary, Luis A., San Marcos, CA, United States
Tarara, Thomas E., San Diego, CA, United States
Kabalnov, Alexey, Corvallis, OR, United States
PI US 2001046474 A1 20011129
AI US 2001-862764 A1 20010521 (9)
RLI Division of Ser. No. US 1998-218212, filed on 22 Dec 1998, PENDING
Continuation of Ser. No. WO 1998-US20615, filed on 29 Sep 1998, UNKNOWN
Continuation-in-part of Ser. No. US 1998-133848, filed on 14 Aug 1998, ABANDONED Continuation-in-part of Ser. No. US 1998-106932, filed on 29 Jun 1998, ABANDONED
PRAI US 1997-60337 19970929 (60)
DT Utility
FS APPLICATION
LREP INHALE THERAPEUTIC SYSTEMS, INC, 150 INDUSTRIAL ROAD, SAN CARLOS, CA, 94070
CLMN Number of Claims: 150
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 2850
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . 1.287

| | |
|---|---|
| CFC-114 | 1.288 |
| PFOB | 1.305 |
| Mannitol | 1.333 |
| Ethanol | 1.361 |
| n-octane | 1.397 |
| DMPC | 1.43 |
| Pluronic F-68 | 1.43 |
| Sucrose | 1.538 |
| Hydroxyethylstarch | 1.54 |

**Sodium chloride** 1.544

DETD . . . amino acids are further held to be within the scope of the present invention. The inclusion of both inorganic (e.g. **sodium chloride**, calcium chloride), organic salts (e.g. sodium citrate, sodium ascorbate, magnesium gluconate, sodium gluconate, tromethamine hydrochloride) and buffers is also contemplated.

DETD . . . inhibitors, e.g. cromolyn sodium; antiinfectives, e.g. cephalosporins, macrolides, quinolines, penicillins, streptomycin, sulphonamides, tetracyclines and pentamidine; antihistamines, e.g. methapyrilene; anti-inflammatories, e.g. **fluticasone propionate**, beclomethasone dipropionate, flunisolide, budesonide, tripedane, cortisone, prednisone, prednisilone, dexamethasone, betamethasone, or triamcinolone acetonide; antitussives, e.g. noscapine; bronchodilators, e.g. ephedrine, adrenaline, fenoterol, **formoterol**, isoprenaline, metaproterenol, salbutamol, albuterol, salmeterol, terbutaline; diuretics, e.g. amiloride; anticholinergics, e.g. ipatropium, atropine, or oxitropium; lung surfactants e.g. Surfaxin, Exosurf,. . .

DETD . . . and osmotic agents (to provide isotonicity, hyperosmolarity, or hyposmolarity). Examples of suitable salts include sodium phosphate (both monobasic and dibasic), **sodium chloride**, calcium phosphate, calcium chloride and other physiologically acceptable salts.

DETD [0173] 3.25% w/v **Sodium chloride** (Mallinckrodt, St. Louis, Mo.)

CLM What is claimed is:

. . . 29. The stable respiratory dispersion of claim 1 wherein said bioactive agents are selected from the group consisting of budesonide, **fluticasone propionate**, salmeterol, **formoterol** and DNase.

. . . 150. The stable respiratory dispersion of claim 133 wherein said bioactive agents are selected from the group consisting of budesonide, **fluticasone propionate**, salmeterol, **formoterol** and DNase.

=> d 7 ab bib kwic

L8 ANSWER 7 OF 10 USPATFULL

AB Stabilized dispersions are provided for the delivery of a bioactive agent to the respiratory tract of a patient. The dispersions preferably comprise a plurality of perforated microstructures dispersed in a suspension medium that typically comprises a hydrofluoroalkane propellant. As density variations between the suspended particles and suspension medium are minimized and attractive forces between microstructures are attenuated, the disclosed dispersions are particularly resistant to degradation, such as, by settling or flocculation. In particularly preferred embodiments, the stabilized dispersions may be administered to the lung of a patient using a metered dose inhaler.

AN 2001:190709 USPATFULL

TI Stabilized preparations for use in metered dose inhalers

IN Weers, Jeffry G., San Diego, CA, United States
Schutt, Ernest G., San Diego, CA, United States
Dellamary, Luis A., San Marcos, CA, United States

Tarara, Thomas E., San Diego, CA, United States
Kabalnov, Alexey, Corvallis, OR, United States
PA Inhale Therapeutic Systems, Inc., San Carlos, CA, United States (U.S. corporation)
PI US 6309623 B1 20011030
AI US 1998-218212 19981222 (9)
RLI Continuation of Ser. No. WO 1998-US20615, filed on 29 Sep 1998 Continuation-in-part of Ser. No. US 1998-133848, filed on 14 Aug 1998, now abandoned Continuation-in-part of Ser. No. US 1998-106932, filed on 29 Jun 1998, now abandoned
PRAI US 1997-60337 19970929 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Bawa, Raj
LREP Rafa, Michael J., Cagan, Felissa H.
CLMN Number of Claims: 93
ECL Exemplary Claim: 1
DRWN 17 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 2644
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . 1.287
CFC-114 1.288
PFOB 1.305
Mannitol 1.333
Ethanol 1.361
n-octane 1.397
DMPC 1.43
Pluronic F-68 1.43
Sucrose 1.538
Hydroxyethylstarch 1.54
**Sodium chloride** 1.544
DETD . . . amino acids are further held to be within the scope of the present invention. The inclusion of both inorganic (e.g. **sodium chloride**, calcium chloride), organic salts (e.g. sodium citrate, sodium ascorbate, magnesium gluconate, sodium gluconate, tromethamine hydrochloride) and buffers is also contemplated.
DETD . . . inhibitors, e.g. cromolyn sodium; antiinfectives, e.g. cephalosporins, macrolides, quinolines, penicillins, streptomycin, sulphonamides, tetracyclines and pentamidine; antihistamines, e.g. methapyrilene; anti-inflammatories, e.g. **fluticasone propionate**, beclomethasone dipropionate, flunisolide, budesonide, tripedane, cortisone, prednisone, prednisilone, dexamethasone, betamethasone, or triamcinolone acetonide; antitussives, e.g. noscapine; bronchodilators, e.g. ephedrine, adrenaline, fenoterol, **formoterol**, isoprenaline, metaproterenol, salbutamol, albuterol, salmeterol, terbutaline; diuretics, e.g. amiloride; anticholinergics, e.g. ipatropium, atropine, or oxitropium; lung surfactants e.g. Surfaxin, Exosurf,. . .
DETD . . . and osmotic agents (to provide isotonicity, hyperosmolarity, or hyposmolarity). Examples of suitable salts include sodium phosphate (both monobasic and dibasic), **sodium chloride**, calcium phosphate, calcium chloride and other physiologically acceptable salts.
DETD Solution 1
3.9% w/v m-HES hydroxyethylstarch (Ajinomoto, Tokyo, Japan)
3.25% w/v **Sodium chloride** (Mallinckrodt, St. Louis, MO)
2.83% w/v Sodium phosphate, dibasic (Mallinckrodt, St. Louis, MO)
0.42% w/v Sodium phosphate, monobasic (Mallinckrodt, St. Louis, MO)

Solution. . .
CLM What is claimed is:
. . . 29. The stable respiratory dispersion of claim 1 wherein said bioactive agents are selected from the group consisting of budesonide, **fluticasone propionate**, salrieterol, **formoterol**, gentamicin, LHRH, and DNase.

. . . 87. The stable respiratory dispersion of claim 72 wherein said bioactive agents are selected from the group consisting of budesonide, **fluticasone propionate**, salmeterol, **formoterol** and DNase.

=>

1: Pharmacoeconomics 2000 Dec;18(6):591-608 Related Articles, NEW Books, LinkOut

# Inhaled salmeterol/fluticasone propionate combination. A pharmacoeconomic review of its use in the management of asthma.



**Markham A, Adkins JC.**

Adis International Limited, Auckland, New Zealand.



Cost estimates from developed countries indicate that asthma accounts for up to 2% of the economic cost of all diseases. A large proportion of asthma-related costs are attributable to poor asthma control. Treatment strategies which improve clinical outcomes in patients with asthma, therefore, have the potential for significant economic benefits, and it is important to evaluate new asthma therapies for cost effectiveness. Several studies have established that salmeterol and fluticasone propionate combined in a single dry powder inhalation device are at least as effective as a combination of the 2 drugs administered via separate dry powder inhalers and more effective than monotherapy with fluticasone propionate or budesonide. Importantly, pharmacoeconomic analysis of several of these studies show that the salmeterol/fluticasone propionate combination is cost effective relative to monotherapy with fluticasone propionate or budesonide. Although the total cost of asthma management tended to be slightly higher with salmeterol/fluticasone propionate than with inhaled corticosteroid monotherapy, in most cases mean cost-effectiveness ratios were lower (i.e. more favourable) for salmeterol/fluticasone propionate than either fluticasone propionate or budesonide. Cost effectiveness was assessed according to 3 end-points: successfully treated weeks, symptom-free days and episode-free days. Mean cost-effectiveness ratios consistently favoured salmeterol/fluticasone propionate over the comparator drug for the end-point successfully treated weeks, and in most cases the other 2 end-points also favoured the combination product over the comparator. In a further study, salmeterol/fluticasone was also less costly than therapy with formoterol and budesonide administered via 2 separate inhalers. Studies of health-related quality of life (HR-QOL) using the Asthma Quality of Life Questionnaire indicate that salmeterol/fluticasone propionate produces clinically meaningful improvements in overall HR-QOL relative to salmeterol monotherapy or placebo. Improvements in overall HR-QOL were statistically significantly greater for salmeterol/fluticasone propionate than with fluticasone propionate or budesonide alone, although the differences between treatments did

not exceed the threshold for clinical significance. In conclusion, short term cost-effectiveness data show that salmeterol/fluticasone propionate is more cost effective than the inhaled corticosteroids budesonide and fluticasone propionate alone. The combination product also appears to improve HR-QOL relative to placebo or salmeterol alone.

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# Dose-response relationships in determining the safety:efficacy ratio.



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The development of inhaled agonists selective for beta 2-adrenoceptors and high potency corticosteroids has improved the treatment of asthma. The delivery of the drugs to the site of action reduces the systemic exposure and hence reduces adverse systemic events. Together, these factors have resulted in improved toxicity: therapeutic ratios. Long-acting beta 2-agonists, such as salmeterol and formoterol, and high efficacy corticosteroids, such as fluticasone propionate and budesonide, now are available for clinical use. Because suboptimal treatment of asthma causes increased morbidity and mortality, and increased costs to society, these compounds are of particular value. Risk factors associated with fatal and near-fatal asthma have been identified, and it would appear that drug treatment by metered dose inhaler per se does not cause increased asthma fatality as an independent risk factor.

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